Diabetologia (1992) 35: 139–142

R79 Key COHORT STUDY 1962-63

Diabetologia

The incidence of male childhood Type 1 (insulin-dependent) diabetes mellitus is rising rapidly in The Netherlands

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Summary. This study evaluates the cumulative incidence of Type 1 (insulin-dependent) diabetes mellitus in male army conscripts 0–18 (inclusive) years of age in the Netherlands (birth cohorts) over 10 years. Data from 2136 cases were retrieved from files of the conscript registry of the Royal Dutch Army. Ascertainment was sought by the capture-recapture method, achieving an average ascertainment rate of 89.7%. Poisson regression modelling was used to determine the change in incidence over time. A significant non-linear increase in the incidence of insulin-dependency in the birth cohorts of 1960–1970 was found. The cumulative incidences of the early birth cohorts 1.85/1000 (1960), 1.76/1000 (1961), 1.11/1000 (1962) were considerably lower than of the later birth cohorts 1.96/1000 (1968), 2.11/1000 (1969), 2.12/1000 (1970). Overall the risk of Type 1 diabetes increased on the average 4.4% with each annual birth cohort. Only for the 1962 birth cohort was a significant dip in the incidence observed. The results indicate a rapidly increasing incidence of diabetes in males in the Netherlands consistent with the concurrent rapid rise in Northern Europe, found in both sexes.

Key words: Type 1 (insulin-dependent) diabetes mellitus, military medicine, incidence, cohort studies, longitudinal studies, child.

During the past decades, surveys in the Nordic countries have found an increase in risk for Type 1 (insulin-dependent) diabetes mellitus [1–3] with an annual change of approximately 3.3%, in Finland 2.4% [4]. Studies in North America however, have demonstrated little long-term variation in the incidence of diabetes [5]. World-wide, there are few data available to evaluate temporal trends for the risk of developing diabetes in the young. In the Netherlands the incidence during 1978–1980 (inclusive) was 11.6/100,000 for males, 0–19 years of age [6]. The current study looked for temporal trends of the incidence of Type 1 diabetes in the 1960–1970 birth cohorts of male army conscripts in the Netherlands [7]. Following the approach by Green and associates [8, 9] in Denmark, the army conscript registry was chosen, as all males aged 18 are eligible for military service by law and most participate in a standardized medical screening programme to evaluate their fitness for service. Thus, a nation-wide source over time is available, in as much as the screening procedures were constant over time.

Subjects and methods

Data were obtained from the files of the National Military Service Medical Examination Office for male conscripts born in the years 1960–1970. The military authorities required that while obtaining the data, confidentiality of the conscripts was respected. The files contain information written by the examining military physician on a standardized form. The medical procedures and forms were introduced in 1955 and are still in use. At the medical examination a special code was given by the military physician to all 18-year-old males who have "diabetes mellitus" and/or "glucosuria". In the large majority, a diagnosis of insulin-dependency was based on written evidence (94%) from either the paediatrician or the internist treating the conscript, or from his general practitioner. In the Netherlands all young Type 1 diabetic patients are treated by a paediatrician or an internist [6] and the general practitioner (family doctor) always receives reports from these specialists.

In 6% of the subjects the military doctor had to confirm the diabetes information from the conscript, when no written evidence was available at the examination. This confirmation included a formal prescription to the conscript for insulin, a confirmatory telephone call from the treating physician and also by observing signs of cicatrization at injection-sites. If glucosuria was detected in a random urine sample on the day of medical examination by simple reduction testing, a standardized oral glucose tolerance test (OGTT) was subsequently performed by an internist at the Central Military Hospital, using 75 g load of glucose after an overnight fast. The results of the test were sent to the referring military physician and, if abnormal, also to the local doctor. These procedures have not been changed since 1955. The results of the OGTT were found in the files of the military registry and all have been interpreted according to the National Institutes of Health criteria by the investigators, the following two criteria established diabetes: 1. After an overnight fast, ve-

Table 1. Classification of army conscripts with primary code "diabetes mellitus" or "glucosuria" on medical examination form, total $n = 2509$ for the birth cohorts 1960–1970 (inclusive)

	n	% of total
Previous insulin-dependency manifest ≤ 18 years of age	2136	85.1
Positive urinary reduction		
diabetic OGTT*	46	1.8
non-diabetic OGTT	291	11.6
Previous diabetic diet and/or oral hypoglycaemic agents	36	1.4

OGTT = oral glucose tolerance test;
* On follow-up through the local physicians, all were prescribed insulin within 1 year after testing, this was not evaluated for the 36 conscripts reportedly taking hypoglycaemic agents or a diabetic diet

nous glucose concentration ≥ 7.0 mmol/l on at least two separate occasions (and/or), 2. Following 75 g of oral glucose: venous plasma concentration ≥ 10.0 mmol/l on at least two occasions during the 2-h test, sampling every 15 min.

Some conscripts are exempted from military service and hence from medical examination because of so-called brother-service: if two older brothers have already completed their military duty, there is exemption for each younger brother. Their percentage, of the total number of annual conscripts, decreased from 6.9% (birth cohort 1960) to 2.3% (birth cohort 1970), reflecting the tendency towards smaller families. Also, conscripts living in foreign countries, staying in prison (convict), in a psychiatric home, or working in sacerdotal office, may not have had a medical examination at age 18. Further, it is conceivable that other disease states, for example chronic pulmonary disease, were considered sufficient for exemption and that an additional diagnosis of diabetes was not noted. Finally, the military registry is incomplete with regard to death prior to the age of 19 years. However, the mortality rates of diabetes, both primary and secondary causes, in 0–19-year-old-boys from 1950–1984, were very low and have changed very little [10]. The average death rate with Type 1 diabetes as a primary cause was 2.1/1,000,000 during this time period [11], and thus would have only a marginal effect on the incidence rates.

To determine the degree of ascertainment and from there to estimate the true number of incident cases in the population, the Lincoln-Peterson capture-recapture method [12] was applied. As a secondary source for validation a former nation-wide actual incidence study was employed of Type 1 diabetes among 0–19-year olds during 1978–1980 [6]. This study obtained data from a questionnaire sent to all physicians involved in the treatment of young diabetic patients, ascertained by sending the same questionnaire to all members of the Dutch Diabetes Association. The degree of ascertainment for paediatricians was 94% and for internal medicine specialists 75%. The data of the former incidence study (recapture) by questionnaire were collected quite differently both in purpose and in timing from the present one (capture), hence suitable for independent ascertainment.

The capture-recapture method was applied for the birth cohorts of 1960–1970. The older conscript birth cohorts 1955–1958 could not be recaptured by the actual national incidence data, collected during 1978–1980, comprising newly-diagnosed cases aged 0–19 years only. Further the total birth cohort 1959 (January–December) was exempted from military service by national decree.

The matching criteria were date of birth and also, available in 33%, the date of the first administration of insulin.

Statistical analysis

The Poission regression model was fit into the adjusted cumulative incidence rates using the statistical package GLIM [12]. This was performed to determine if there was a statistically significant increase over time [13]. The risk of developing diabetes under the age of 19 in a population of Dutch males could only be modell function of birth cohorts. Age and calendar time of onset of di could not be modelled because of incomplete data concerni date of first administration of insulin. The linear model was fi the data in the following order [14]. The dependent variable. justed cumulative incidence, was first introduced to the mod ond, the independent variable, birth cohort, was fitted to the without including a term for trend.

Results

Table 1 depicts the population initially coded diabetes or glucosuria in the military registry, $n = 25$[...] sulin-dependency before age 19 years was documen 2136 subjects, born between 1960–1970. In 46 cons the finding of a diabetic OGTT was followed by pre ing insulin within 1 year after the finding of positive tion in the urine at the initial medical military ex ation. This would represent only 1.8% of the population found insulin dependent then.

The descriptive analyses of the ascertainment-ad cumulative incidences are shown in Table 2. It ap that the cumulative incidence increased from 1.85 (to 2.12 (1970). The ascertainment from the previc cidence study into the military records ranged fron to 100%. In the birth cohorts of 1963 and 1969 all could be recaptured, for 1962, 75% was found, the age for all birth cohorts was 89.7%. The low rate birth cohort of 1962 was the only one significantly ent ($p < 0.05$) after adjusting for ascertainment upon the 95% confidence intervals, despite its rel low degree of ascertainment (75%).

Figure 1 represents the temporal trend of insul pendency by the calculated mean annual inciden each birth cohort by age 18 years. Increases were ways present in each subsequent year of birth, b overall trend did show an increase in incidence of diabetes for birth cohorts of 1960–1970 of 4.4% anr

Comparing the deviance with the appropriate d of freedom before and after fitting the birth cohorts model for linearity revealed that the model itself w accepted ($p < 0.001$). This implies that although the

Table 2. Cumulative incidence of Type 1 (insulin-dep diabetes mellitus in male army conscripts aged 18 years

Year of Birth	National number of 18-year-old males	Noted insulin-dependent in the Military Files	Ascertainme adjusted cum incidence pe (95% confid intervals)
1960	119761	189	1.85 (1.60–2.
1961	123393	167	1.76 (1.52–2.
1962	122783	96	1.11 (0.92–1.
1963	125069	188	1.50 (1.30–1.
1964	125955	198	1.83 (1.59–2.
1965	122978	203	1.93 (1.68–2.
1966	119880	184	1.71 (1.48–1.
1967	119659	219	2.07 (1.81–2.
1968	118716	194	1.96 (1.70–2.
1969	124893	264	2.11 (1.87–2.
1970	120634	234	2.12 (1.87–2.

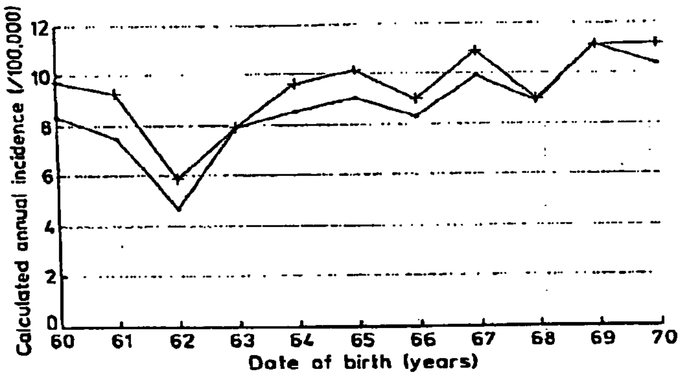

Fig. 1. Temporal trend in the annual cumulative incidence of Type 1 (insulin-dependent) diabetes mellitus in male army conscripts in the Netherlands across birth cohorts, 1960–1978, 1961–1979, etc. Military (–●–) represents the data from the registry proper, adjusted (–+–) implies the annual cumulative incidence after correction for ascertainment. Overall a non-linear increase in incidence for the birth cohorts 1960–1970 was observed. A significant ($p < 0.05$) decline for cohort 1962 was seen after adjusting for ascertainment

a significant increase in the incidence of Type 1 diabetes over the total observed period, the increase did not follow a linear trend ($p < 0.05$). The beta coefficient was 1.2/1000 per birth cohort year, or a 4.4% increased incidence for each yearly birth cohort. Also, after exclusion of the birth cohort 1962 the upward trend remained significant.

Discussion

The population obtained from conscript data represents a fairly complete nation-wide sample of all Type 1 diabetic males in the Netherlands born between 1960–1970, confirming earlier data from Denmark [7]. A significant non-linear increase was found in the cumulative incidence of Type 1 diabetes. The overall increase could not be attributed to factors leading to a "false" rise such as under-ascertainment, improvement of diagnosis or registration, changes in case definition, or disease-associated death.

No appeerent slow-down at the end of the present survey was observed. If this trend were to continue, there would be a doubling in incidence every 20–25 years. This increase in cumulative incidence seems in keeping with the annual increase of 3.3% in actual incidence [5] observed in other northern European countries for both sexes. It must be understood however that cumulative incidences for birth cohorts are not directly comparable to actual incidences.

Increases in actual incidence have been seen in Sweden [1], Norway [2], Finland [3], New Zealand [5], Austria [16], Denmark [17], France [18], Luxembourg [19] and Poland. Little or no temporal change has been found in Scotland [20], Spain [21], Canada (Montreal, Prince Edward Islands) and in the United States (Allegheny County (Pennsylvania), North Dakota, Colorado and Monroe County (New York State)) [5]. In Leicestershire (United Kingdom) [22] inconsistent trends have been observed. In addition the differences in cross-sectional incidence rates between the different countries remain striking, as in Nordic countries the incidence rate is 20–30/100,000 per year whereas in Japan the rate is 1/100,000 per year [23]. An apparent epidemic of clinical manifestation has been reported from midwestern Poland [24].

On the other hand, a report from the United Kingdom [24] suggested that the overall cumulative incidence of early-onset diabetes has not increased, but that the disease is expressed clinically at an earlier age. Different ways of estimating incidence may well lead to different interpretations with regard to temporal trends [13].

Five previous studies have evaluated temporal trends in Type 1 diabetes by birth cohort. Data from Denmark have indicated a significant rise in incidence for the birth cohorts 1949–1956 [17]. However, studies from the United States [5], Poland [24], Sweden [26] and Finland [27] failed to do so. Given the lack of evidence for effects of birth cohorts found elsewhere, we plan to examine whether the age at which Type 1 diabetes became clinically manifest was different between the present, relatively large birth cohorts and also changes with time across the age groups (0–18). At this point there is no way to decide whether the intruiging dip in cumulative incidence for the 1962 birth cohort was due to chance or associated with features of clinical manifestation.

We confirm that military conscript health data may be considered for monitoring the cumulative incidence of insulin-dependency (and perhaps of other easily defined chronic childhood disorders). It is our impression that the procedures for military service health assessment in the Netherlands is similar to that in other countries and that these procedures have not changed much over time.

Acknowledgements. We thank Dr. A. Green, Odense, Denmark, Chairmen of Eurodiab subarea A for epidemiologic studies, for his critical reading of the manuscript and Mrs. J. Drost-v. d. Linden and Mrs. M. Huls-van Vliet for secretarial help. The study was supported by the Dutch Diabetes Research Fund, the Child Health and Wellbeing Fund, Rotterdam and the National Institutes of Health, grant DK 24021. CEMD received a student-travel grant from the State University of Groningen (Prof. HSA Heijmans, Department of Paediatrics).

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Received: 11 June 1991
and in revised form: 27 September 1991

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